

CLAIMS

1. Agglomerates in crystalline form comprising one or more β -lactam
5 compounds, wherein at least one β -lactam compound has a high water
affinity, and optionally containing one or more excipients, with the proviso
that the rosette-like crystalline form of potassium clavulanate is excluded.

2. Agglomerates according to claim 1, wherein the agglomerates are
10 substantially free from non-agglomerated β -lactam crystals.

3. Agglomerates according to claim 1 or 2, wherein at least one β -
15 lactam compound is clavulanic acid.

4. Agglomerates according to any one of the claims 1-3, wherein the β -
lactam compound is potassium clavulanate.

5. Agglomerates according to claim 4, consisting of only potassium
20 clavulanate.

6. Agglomerates according to claim 4 further comprising amoxicillin.

7. Agglomerates according to anyone of the claims 1-4 or 6, wherein
25 the excipients are microcrystalline cellulose, preferably Avicel®, or silica,
preferably Syloid® or Aerosil®.

8. Agglomerates according to anyone of the claims 1-7, wherein the
agglomerates have an average particle size between about 1 μm and 1500
30 μm , preferably between about 500 μm and 1500 μm , more preferably
between 800 μm and 1200 μm , or preferably between 1 μm and 300 μm ,
more preferably between 1 μm and 200 μm .

9. Agglomerates according to anyone of the claims 1-8 in sterile form.

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5 10. A process for the preparation of crystallised agglomerates as defined in anyone of the claims 1-9, wherein the agglomerates are produced in a liquid phase by applying stirring devices.

10 11. A process according to claim 10, wherein the liquid phase comprises a solution or suspension of at least one corresponding β -lactam compound in a solvent or in a mixture of solvents together with one or more anti-solvents.

15 12. A process according to claim 11, wherein the ratio of the weight of the solution containing β -lactam compound to the anti-solvent is about 0.05 to 10 wt.%.

20 13. A process according to claim 11 or 12, wherein the solvent is selected from the group consisting of water, alcohol, ketone and ester or a mixture thereof, whereby water is present.

25 14. A process according to anyone of the claims 10-13, wherein the anti-solvent is a ketone, like acetone, methylethylketone, methylisobutylketone or an ester, like methyl acetate, ethyl acetate, isopropyl acetate, butyl acetate or an alcohol, like 1-propanol, 1-butanol, 2-butanol, 2-methyl-1-propanol or a mixture of these solvents, optionally containing water.

30 15. A process according to anyone of the claims 10-14, wherein one or more stirring devices are used to crystallise, agglomerate and/or deagglomerate the β -lactam compound and optionally classification and blending with excipients and/or another β -lactam compound in a batch or continuous operation, in one or more units.

16. A process according to claim 15, wherein the process is performed by applying stirring devices in one or more vessels, in-line mixers or a combination thereof.

5 17. A process according to claim 15 or 16, wherein a high shear mixer is used as stirring device.

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10 18. A process according to anyone of the claims 10-17, characterised by the preparation of agglomerates with various particle sizes, by further using a combination and permutation of different stirring devices and their speed, the type and amount of the solvents used and the way of mixing of one or more solvents and anti-solvents.

15 19. A process according to claim 18, characterised by the preparation of agglomerates with various particle sizes, by further using a nozzle-sprayer for the solution.

20 20. A process according to any one of the claims 10-19, characterised by dissolving one or more corresponding β -lactams in a solvent, adjusting the pH to about neutral and mixing with the anti-solvent.

25 21. A pharmaceutical formulation comprising the agglomerates of anyone of the claims 1-9 and one or more pharmaceutical acceptable excipients.

30 22. A pharmaceutical formulation comprising amoxicillin, preferably amoxicillin trihydrate and the crystalline agglomerates of potassium clavulanate as defined in claim 5, and optionally one or more pharmaceutically acceptable inert excipients.

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23. A pharmaceutical formulation, comprising a mixture of amoxicillin trihydrate and crystalline agglomerates of potassium clavulanate and one or more pharmaceutically acceptable inert excipients as defined in claim 4.

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24. Pharmaceutical dosage form comprising a pharmaceutical formulation of anyone of the claims 21-23.

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